THE EFFECT OF CONTINUOUS VENO-CLYSIS IN THE TREATMENT OF INTESTINAL INTOXICATION IN INFANTS

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Within the last two decades the mortality rate in summer diarrhoea has been greatly reduced due to a pure milk supply, education of mothers in the principles of feeding and hygiene, better housing conditions and improved treatment. To further reduce the mortality rate in summer diarrhoea much work has been done to determine the etiology of the disease in the hope of developing a specific treatment. In spite of all this work the true etiology of this disease has not been found. The most important theories are as follows:

(1) The available data to date shows that primary bacterial infection is unlikely. Various organisms have in turn been indited. The colon baccilli Erchefrich, Morgan's bacillus, bacillus protens, Booker, B. Welchi Kendall, to mention a few. Such organisms have been found in the stools of normal infants, Blackfan, Davison, and it has been found that many of these bacilli were not agglutinated by the sera of patients suffering with diarrhoea, Tenbroech, which indicates that it is not known just what the etiologic relation of a specific bacterial infection is to diarrhoea.

(2) The role of parenteral infection as otitis media and mastoiditis has been over emphasized, Marriott, Floyd, and it is the general experience that only a small per cent of cases with diarrhoea can be attributed primarily to this cause. Indeed, summer diarrhoea may be successfully treated by conservative

measures in the presence of such infection.

(3) Reduction of gastric acidity and motility and the reduction of gastric and duodenal enzymes with subsequent fermentation of undigested and unabsorbed foods by the endogenous stool organisms giving irritating ends products causing diarrhoea has been brought out by Davison. He seems to have shown that these organisms ascend into the upper intestinal tract and multiply because of reduced acidity and enzymes, thus causing diarrhoea.

(4) External Heat. That external heat or atmospheric temperature bears a definite relationship to summer diarrhoea has been known for years. The name summer diarrhoea is in itself indicative and the causative relationship is evidenced by the common occurrence of epidemics in the hot American cities. Fewer cases are seen in England and other cooler climates. In Scotland Thompson says, "Severe outbreaks of summer diarrhoea are very rare." Davison thinks the heat acts by depressing gastric secretions and disturbing metabolism and is the predisposing cause.

(5) Recently Dodd and co-workers have shown that in severe cases of alimentary intoxication there is an unknown toxic substance which might cause irreparable damage to the tissues. The presence of this toxic agent guanidin or guanidin-like substances in the blood was claimed to be responsible for their high death rate until calcium gluconate was used as an antagonistic to guanidin. More definite evidence is necessary to substantiate this theory.

(6) Finkelstein thought the salts and then the carbohydrates were the main cause of diarrhoea and this has been discarded.

(7) The important predisposing factors in diarrhoea such as impure milk supply, bad housing conditions, poverty, neglect, ignorance, previous debility of the infant are recognized.

In the last three decades these problems have been attacked with a resultant great reduction in mortality in infants from summer diarrhoea yet in summing up the etiology one can go back 50 years and say with Henoch that "the nature of the disease is, however, entirely unknown."

Shick thinks that once the diarrhoea is started there is set up a non-specific irritation of the nervous apparatus of the gastro-intestinal tract which is aggravated by giving anything by moutn.

From the therapeutic viewpoint, many forms of treatment have been advocated at different times following the accepted theory of causation at that time. They have been partially successful but after each trial of a particular method or variation in treatment there has always been a return to purely symptomatic treatment.

Using conservative accepted methods of treatment in an epidemic in the South in the summer of 1931 our mortality was approximately 45%. The treatment consisted of withdrawal of all food for a period of 6-24 hours, giving liberal quantities of fluid orally and parentally, plain boiled water, weak tea, barley water and normal sodium chloride, Ringers or Hartman's solution by hyperdermo-clysis, or the intraperitoneal route. Blood transfusion by the multiple syringe method was also used. When the toxicosis, skin turgor and stools showed improvement, skim milk mixtures P.P.M. (Powdered Protein Milk) or cereal preparations were begun and gradually increased.

Power's mortality in a series of cases in 1926 was 33% despite every approved method of treatment including water diet, fluids by all routes, blood transfusions and careful after feeding. Without the use of a comprehensive plan in 19 cases the mortality was 70%.

At the New York Nursery and Child's Hospital between 1925 and 1928 in 175 cases there was a mortality of 35%. Hartman in 1928 in 27 cases had a death rate of 88%. Hoag and Marples in 1931 using a plan somewhat similar to Power's had in 14 cases a mortality of 29%. Karelitz's and Schick's mortality in the summer of 1930 with 21 patients was 14% thereby reducing the mortality rate at Mt. Siani Hospital over a ten year period from 64 to 14%. The method of treatment in their cases was by continuous intravenous infusion or veno-clysis. In a recent report by Cohen of 9 cases of intestinal intoxication treated by veno-clysis the mortality rate was 22%.

This paper is a report of the theory methods and results obtained in a series of 8 cases of intestinal intoxication treated by continuous veno-clysis as originated by Hendon for surgical cases and modified by Karelitz and Shick for use in cases of summer diarrhoea or alimentary toxicosis in infants. The cases, [redacted] were treated in the Children's Hospital, Denver Colorado, where I was Chief Resident Physician in the late summer of 1932. The provisions of a large endowment for this institution forbade research work. This prevented our obtaining any worth while data on the chemistry of the condition during the disease so we decided to confirm and utilize clinically the claims of Karelitz and Shick.

The treatment varied in minor details in each case due to the condition of the patient and divided opinions among the senior

staff physicians as to details of the proceedure. This afforded some interesting and practical observations. The results in our series were gratifying.

Report of a Case

Roy H.S., age 7 months was the second child. Full term, normal labor. Birth weight 5 lbs. 10 oz. Breast fed 2 months at 3 hour intervals, 7 feedings in the 24 hours. Breast milk was insufficient and complemental feeds were given twice a day at 3 and 9 p.m. consisting of evaporated Pet milk 3 oz., water 6 oz., and Karo 2 teaspoons, the quantity varying or adjusted to age and desire for food. Weaned at 2 months and the same formula as above continued up to 10 days before admission, giving 6 feedings a day at 3 hour intervals. The infant had received orange juice and cod liver oil in suitable amounts from the third month. He had been perfectly well up to onset of present illness.

Two weeks before the admission (on September 5, 1932) the infant began to have frequent stools, 3-4 a day (there was apparently no preceding dietary indiscretion or infection). The stools increased in frequency to 10-12 a day and for the last week have contained mucus and for the past 2 days streaks of blood. On three occasions he vomited, always at feeding time. There had been fever for several days and the infant has lost considerable weight during the past week. His former weight was said to have been 16 lbs. Present weight is 13 lbs., 6½ oz. Two days after the onset of the diarrhoea the evaporated milk mixture was made very weak and this formula was continued for 5 days. The following 4 days he received boiled water and tea only and was then put on a P.P.M. mixture which was continued

up to the time of admission on 9-5-32. The examination showed a well developed fairly nourished infant with depressed fontanelle and dry inelastic skin. He was drowsy and seemed to show a moderately severe degree of intoxication. Pulse rate 120 and feeble. Remainder of the examination was negative. Routine laboratory work showed: Urine acid, albumin trace with a few hyaline casts and occasional bacteria, acetone negative. Blood, hemoglobin 72%, R.B.C. 3,5000,000, W.B.C. 13,000, P 36, L 60, Mono 3. Coagulation time was 3½ minutes. Temperature 101. The following was the daily progress of the infant.

9-5-32 Colon irrigation with normal saline with some return of mucous. Hartman's solution 150 cc. by hypodermoclysis, P.P.M. 1 tablespoon to 5 oz. H_2O 4 hourly, H_2O ad libidum.

9-6-32 Hartman's repeated. Mantoux test 1/100 negative. Infant drowsy, regular but heavy breathing. Emesis of 1-4 oz. following several feeds. Stools 12 liquid green with mucous. Temperature 102.2. No improvement in condition.

9-8-33 Casec oz.1 added to each feeding. Color poor, ashen to cyanotic, some coughing, breathes heavily. Vomiting continues.

9-9-32 Stools 9, contain mucous but no blood. Emesis of entire formula at 1 p.m. feeding. Drowsy, toxic, rolls eyes about, sclerae dry. X-ray of chest negative.

9-10-32 Casec discontinued. Abdomen doughy. Child restless and toxic. Fontanelle depressed.

9-11-32 Very drowsy and toxic. Eyes sunken. Sclera lustreless. Abdomen doughy. Stools 8, several streaked with blood. Patient's blood typed and matches and 160 cc. of whole uncitrated blood was given by direct multiple syringe method. Marked reaction following

transfusion, the temperature rising two degrees, thirty minutes after and patient chilling with cyanosis and imperceptible pulse. External heat applied. Adrenaline 3 minimums given and in one hour condition had improved.

9-12-33 Patient looks moribund this morning. Marked dehydration and toxicity. Skin and subcutaneous tissues have a peculiar resistant feel, parchment like and tense over entire body especially over the chest. Resembles sclerema or scleroderma, in hydrocephaloid state of Hall. Both ear drums injected but not bulging. Takes P.P.M. formula and H_2O poorly. Emesis once. Stools less. Veno-clysis started at 4 p.m. following the technique outlined below, using normal saline plus 5% glucose plus adrenalin $\frac{1}{4}$cc. to 250 of the solution. Phenol barbitol gr.$\frac{1}{4}$ for restlessness. One hundred cc. solution ran in first hour, then 10 drops per minute or 40 cc. per hour as a constant veno-clysis. Nothing by mouth, not even water, for 12 hours. Only a little water to moisten lips and mouth.

9-13-32 Patient looks better this morning. Turgor improved. Temperature to normal. Only two stools during the night. Slept well. Veno-clysis continued at 40 cc. per hour. Water begun by mouth, 20 cc. 2 hourly.

9-14-32 Some cough. Temperature up to 102.4. Slight swelling over right mastoid area. Right drum slightly injected and bulging. Only two stools in past 24 hours. No vomiting. Turgor continues to improve. General condition improved and the patient is less toxic.

9-15-32 Bilateral myringotomy. Pus from both ears. Hot magnesium sulphate packs to right mastoid region.

9-17-32 Temperature normal. Only 1-3 stools per day, no mucous or blood. Ears draining. Mastoid swelling has subsided. Has maintained the 1 lb. weight gained during veno-clysis. Taking 6 oz. formula 4 hourly. Doing well.

9-22-32 Continues to improve. Skin turgor normal. Stools normal. Gaining weight very slowly. Diet for age. From this point on made an uneventful recovery. Discharged 10-5-32. Weight on discharge 15 lbs.

Comment

A severe case of intestinal intoxication treated with the approved methods for 2 weeks including 1 transfusion of whole ancitrated blood of 160 cc. On the 15th day of the disease, the 8th hospital day, the infant was so critically ill that continuous veno-clysis was resorted to. The infant was much improved the following day and went on to a complete recovery. During the veno-clysis of 40 hours there was a weight gain of 1 lb. which was maintained after the veno-clysis was discontinued indicating a rather complete absorption and utilization by the tissues of the solution of the electrolytic given slowly by the intravenous route.

The course of the case was complicated by the occurrence of a bilateral otitis media and a moderate degree of pharyngial and bronchial irritation. It is possible that the otitis media had an etiological bearing on the case but there was no evidence of this infection the first 21 days of the illness and it is more likely that the infection was secondary to the intestinal intoxication. The ear infection probably kept the temperature elevated in the mid course of the disease. It is to be noted that parenteral

fluids were not required following the veno-clysis. A record of the fluid intake in this case is appended.

Method

The evident degree of toxicity varied at the time of admission and the more approved conservative methods of treatment were temporarily adopted in apparently mild cases until the patient was critically ill and then veno-clysis was used.

The procedure was based on the method of Karelitz and Shick and can be briefly stated. Admission preferably to a "private" room was followed by physical examination, laboratory tests, blood matching and set-up of veno-clysis when ordered. During the first hour the rate of flow was 25-30 drops per minute or 100-120 cc. per hour. It was then regulated to 10-15 drops per minute or 40-60 cc. per hour and continued for 30 to 40 hours or till detoxification was complete. No fluid was given by mouth for 12 hours except to moisten the lips and mouth. Twenty cc. of water was then given 2 hourly until the veno-clysis was discontinued. The temperature was taken by axilla. The nurse watched the patient carefully but disturbed him as little as possible. For restlessness codein or luminal was given.

On discontinuing the veno-clysis feeding was begun with a weak milk mixture preferably powdered protein milk 1-4 with saccharine starting with 10cc. 2 hourly, 10-12 feeds in 24 hours and increasing 10 cc. every 2 hours up to 90-120 cc. a feed. The interval was then lengthened and the strength increased gradually. During convalescence parenteral fluid was administered depending on the skin turgor.

FLUID ANALYSIS OF A CASE - Roy H.S.

Day	Oral in Cc. Formula	Oral in Cc. Water	Subcutaneous in Cc. Normal Saline or Ringers	Intravenous in Cc. Normal Saline 5% Glucose	Blood in Cc.		Total in Cc.
1	330	0	150	0	0		480
2	840	270	150	0	0		1260
3	900	360	280	0	0		1540
4	900	240	175	0	0		1315
5	1020	165	250	0	0		1415
6	750	225	200	0	0		1175
7	720	120	150	0	160	(1st-12 hrs - 600	1150
8	450	120	No H_2O by mouth for 12 hours 0		0	(2nd-12 hrs - 425 (3rd-12 hrs - 425	1025
9	0	240	0		0	(4th-12 hrs - 110	775
10	720	240	0		0		960
11	960	210	0	0	0		1170
12	900	285	0	0	0		1185
13	780	300	0	0	0		1080
14	915	450	0	0	0		1365
15	1140	345	0	0	0	In most cases parenteral fluid was given	1485
16	1260	285	0	0	0	for several days	1545
17	1260	400	0	0	0	following the venoclysis	1660
18	1050	240	0	0	0		1290
19	1050	480	0	0	0		1530
20	1050	480	0	0	0		1530
21	1080	500	0	0	0	Note: Fluid days from	1580
22	1140	240	0	0	0	5 A.M. to 5 P.M.	1380
23	Maint.Diet						

Blood transfusion was given at any stage where indicated but usually shortly after beggining the veno-clysis.

T-Board - Restraining the Patient

To insure proper restraint of the patient we adopted the use of a T-board modified after the one originated by Mr. Dennis Brown. The Board was made of two pieces, an upper cross piece at a right angle to the body which is detachable and a body piece, the lower 2/5 of which was in the form of a narrow Y. There were three lengths of T-board to accommodate infants of different sizes. The The board was made of a strong, yet thin 3-ply cross woven wood which resists bending. It was covered with the best quality of moderately soft sponge rubber $\frac{1}{2}$ inch in thickness. The infant was adjusted to the board as described below. We had no complications in using this form of restraint such as hypostatic pneumonia, "bed" sores, etc., and there was the certainty that the infant would not disconnect the glass connection cannula from the intravenous needle or malalign it with the vein through kicking. Altogether we found this the most satisfactory arrangement for restraint of the patient though we think Brush's method is good.

Technique of Veno-clysis

The infant is tied to the T-board by a nurse using cotton as padding under the popliteal fossae and between the Board and leg so that the leg will not be in a strained position in too great extension. A two inch bandage is applied in the mid-thigh region and just below the knee thus strapping the legs firmly to the Board. The leg to be used for the veno-clysis is slightly everted in order to more clearly expose the site where the introduction of

of the cannula is to be made at the lower end of the small saphenous vein.

The arms are placed in a comfortable position some 6 inches from the sides, the hands semi-supinated. A double loop of 2 inch gauze is passed around the wrists and one end of the gauze tied to the cross piece of the Board. This leaves the arms reasonably free yet there is no danger of treatment being interferred with. A small pillow may be placed under the head for additional comfort though this is not essential. Usually we wrapped a towel around the abdomen and under the Board to insure quiet in the early stages of veno-clysis. A napkin was used for excretion and the child could be lifted when a change was necessary.

Of the easily accessible veins we prefer the lower end of the small saphenous as it is constantly placed antero-lateral to the medial malleolus. In small infants we always cut down and tie in the cannula. We find it far more satisfactory than an uncertain vein puncture for a slow continuous infusion and, as a larger cannula can be used it is far less likely to clog. Cannula patency is tested with normal saline and the flow begun. After this one places a sterile pad soaked in alcohol over the wound area and covers this with a sterile towel.

The infusion jar in the Kelly warmer is hung as shown in the photograph and the rubber tubing leading from the Murphy drip bulb to the intravenous cannula is taped to the bed and adjusted so as to give the least possible tension on the cannula in the vein.

Good nursing is essential and the nurse is instructed

to watch the rate of flow, the level of fluid in the Murphy bulb and the temperature of the solution. She should keep an exact record of the quantity of fluid taken hourly and daily by the intravenous route using a separate fluid record sheet, and a record of the fluid or liquids given orally, intervals, amounts, how taken and its effect on the infant. All fluids given orally should be given slowly. She should watch for any symptoms or signs that may be the results of the veno-clysis or of a complication such as edema of any part of the body, local reaction at the site of incision or swelling of the leg on that side, cyanosis or change in color and rapid pulse from too rapid a flow, or vomiting, restlessness, cough, rate and character of breathing, etc., as each of these observations may indicate some advisable adjustment in the treatment. She should see that the flow is maintained, a temporary rise in venous pressure may offer some resistance to the flow and this is shown first by a rise of the fluid level in the Murphy drip bulb and second by some reflex of blood visible in the glass adaptor which fits into the intravenous cannula. In this case the nurse may first raise the heighth of the infusion jar ½ to 1 foot and then she may milk the rubber connecting tube below the Murphy drip bulb intermittently for 5-10 minutes. This is frequently all that is necessary. If the retarded flow is due to some slight angulation of the intravenous cannula it may be necessary to have this corrected.

Preparation of Rubber Tubing and Apparatus.

The new rubber tubing which is 3/16 bore, 1/8 wall pure gum rubber is kneaded with the fingers while being washed thoroughly with soap and water. (This dislodges any foreign particles which

may give rise to a reaction during the veno-clysis). The tubing is then rinsed in water and autoclaved for 15 minutes at 15 pounds pressure. Subsequently sterile sodium chloride is run through the Kelly infusion bottle and the tubes before the apparatus is set up for use.

The veno-clysis set is listed below, photographs of our set-up shown and several drawings of methods included.

Veno-clysis Set

Sterile Pack

Gown with Hand towel

Long towels - - - - - - 4

Flats 4 x 4- - - - - - 24

Applicators - - - - - - 4

Small abdominal sheet - 1

Stockinette - - - - - - 1

Pack sheet- - - - - - - 1

Gloves & glove powder - 1

Other Articles

1. Kelly infusion bottle with 4 ft. rubber tubing, clamp & Murphy drip bulb and adaptor.
2. Kelly warmer
3. Thermometer
4. Kelly stand
5. Sterile graduate
6. Flasks, normal saline
7. T. Board
8. Two inch bandage
9. Cotton wool

Sterile Tray

Sponge sticks - - - - - - - - - - 2

Mosquito forceps- - - - - - - - 4

Toothed thumb forceps - - - - - 2

Mayo Scissors- - - - - - - - - - 1

Cuticle scissors- - - - - - - - 1

Bard Parker Knife - - - - - - - 1

Aneurism needle - - - - - - - - 1

Needle holder- - - - - - - - - - 1

20cc. luer syringe & rubber adaptor - - - - 1

Hypo needles - - - - - - - - - - 2

Recipient needles (#18 & 19) - 2

Rubber adaptors - - - - - - - - 2

Cambric needle- - - - - - - - - 1

Keith straight- - - - - - - - - 1

00 plain catgut - - - - - - - - 1

Dermal and Silk - - - - - - - - 1

Medicine glass (Novocain) - - - 1

Cups (Iodine & Alcohol)- - - - 2

Small basin (Normal saline) - - 1

Other Articles	Sterile Tray
10. 1-litre bottle	Cotton balls - - - - - - - - - 6
11. Glucose (Chem.pure)	Cap for Kelly bottle - - - - 1
12. Epinephrine 1/1000 Several 1 cc. ampoules	

The glass connection tube at the end of the rubber tubing fits into the recipient needle. This has the advantage that the flow is in sight at the point of entrance into the vein and any rise in venous pressure or any blocking of the cannula is shown at once.

Choice of Solution

For any substance to be used intravenously it should be in perfect solution, sterile and compatible with the blood stream. Normal saline is used as a base for nearly all solutions. It is merely an electrolytic base for the carrying of water forming a solution which will not haemolyze the red cells nor irritate the vessel walls. Hendon first used normal saline for continuous venoclysis in 1924 and found it satisfactory in a large series of surgical cases. Shick noted no difference in the reaction to .7 sodium chloride and Ringers solution. Hartman objects to sodium chloride on the basis that intravenous sodium chloride increases the blood chlorides at the expense of the bicarbonate ions which increases the acid ions in cases of severe diarrhoea. He thought that the administration of sodium chloride in the presence of continued oliguria would lead to a more rapid loss of sodium than chlorine ions through the blood which would lead to acidosis.

Hoag, however, in a series of cases, 14, found that

vigorous treatment with parenteral fluids including large amounts of sodium chloride produced no significant elevation of the chloride content of the blood. The treatment resulted in clinical improvement and tended to correct the acid base balance. In none of his cases was there an abnormal accumulation of chloride and a loss of bicarbonate. The treatment did not increase the relative loss of fixed base. Due to an increased urine output, the increased acid excretion compensated for the fixed base lost in diarrhoea.

Hoag thought Hartman's series of cases not convincing on analysis and that too much emphaiss had been placed on the seriousness of the oliguria except in moribund patients.

Powers has found sodium chloride an acceptable solution giving satisfactory clinical results.

Hamilton thought the variation from normal chloride content of the blood was about equal in either direction.

Holt points out that in diarrhoea there is a great draining away from the tissues of both salts and water particularly sodium chloride.

Shick found that those infants with hyperchloremia on admission improved and showed reduction of blood chlorides despite the administration of sodium chloride.

Hartman's solution composed of sodium lactate in a hypotonic base furnishes basic ions unaccompanied by fixed acid ions. The proportion of salts is theoretical as the knowledge of electrolytes lost from the body normally and in diarrhoea is still inadequate. Hartman thinks that with the continuous use of sodium chloride, glucose and alkali intravenously, it is possible to keep the acid base and water

balance more or less normal with frequent blood chemistry check-ups while with his solution this is not necessary owing to the presence of sodium lactate which is converted at a relatively slow but still sufficiently effective rate into sodium bicarbonate which may be retained if needed or excreted if not and because of the solution's hypotonicity it tends to dilute the body fluids and promote diuresis when given in sufficient amounts." "Alkalosis need not be feared if urinary secretion is re-established and kidney function is more or less normal." As Hoag pointed out sodium chloride plus glucose is eminently satisfactory and the essential thing is to use sufficient fluid to re-establish kidney function while glucose is anti-ketogenic.

Ringer's solution has the mineral elements of the blood plasma in approximately the same ratio as found in the blood serum, and the calcium contained in the solution has a stimulating effect on the heart muscle. Theorectically, Ringer's should be more suitable as it contains more electrolytes which would help prevent rapid dissociation and thus replace the electrolytes lost in diarrhoea. But as Powers states, "the most effective solution of electrolytes to administer to patients with intoxication is not known."

Gamble, McKhan, and Butler in investigating the character of the electrolytes in diarrhoeal disease in 2 cases found the loss of phosphates relative to loss of sodium greater than could be explained on the assumption that the loss of fluid in diarrhoea is entirely extr-cellular and the loss of potassium greater than explained by fasting and destruction of protoplasm. They thought this loss of potassium represented a deduction in volume of intracellular fluid. Thus they concluded the use of potassium and sodium in solution for dehydration was supported by their study

and it could be used in weak solution for intravenous use.

Five per cent glucose chemically pure in distilled water is an isotonic solution. This solution has been used with good results in continuous veno-clysis in many hospitals. Matas in 1923 was its first real advocate. It is nutritive, it combats acidosis, aids diuresis and enables the physician to be independent of the gastro-intestinal tract for this type of nourishment. A long period of oral starvation can therefore be used as a valuable therapeutic measure. Hendon has shown this in the report of some of his cases.

Woodyat has shown that glucose is readily utilized by the intravenous route and that a normal rabbit, man or dog can utilize between .8 and .9 grams of glucose per Kg. body weight an hour without glycosuria for an indefinite time.

Considering the above we decided to use glucose 5% in normal saline, a slightly hypertonic solution to which we added ½ cc. of 1/1000 adrenalin to each 500 cc. The adrenalin serves to combat any circulatory collapse in diarrhoeal patients.

Administration of Fluid

Veno-clysis offers besides its therapeutic advantage a superior route of administering fluid to an infant. Hypodermoclysis with repeated needle punctures is painful, disturbs the patient, stretches the subcutaneous tissue, and may lead to infection and only a moderate amount of fluid may be absorbed in the presence of circulatory stasis.

Proctoclysis disturbs the patient and is uncertain in its action in regard to absorption. The intra-peritoneal route is contraindicated in the presence of distension and is not without a real

element of danger as shown by Ravanel due to puncture of the infant's epigastric artery or to peritonitis.

Transfusion

Brown was the first to report the benefits of blood transfusions in children on a large scale in 1921. In his series of 108 cases of acute intestinal disturbances including fermentative diarrhoea, infectious diarrhoea and acute intestinal intoxication there was a mortality of 59%, while in another group of cases treated without blood transfusion the mortality was 84%.

Powers is of the opinion that blood transfusion is the most valuable single measure of all the therapeutic aids. In his cases there were few untoward reactions, the reactions occurring usually in those patients with marked malnutrition accompanying the intestinal intoxication. The reactions were minimized by giving the transfusion 1-2 hours after the administration of parenteral fluids.

Sidbury, in a series of 25 cases of acute intestinal intoxication had a mortality of only 20% using parenteral fluids followed by blood transfusion. He considers blood transfusion just as much an emergency in some of these cases as a ruptured appendix.

How transfusion acts we do not know, the benefit may be due to mechanical action, like a viscus fluid being added to the blood stream, to the antibodies it contains, or to the hemoglobin content.

Our transfusions were given by the multiple syringe method.

Treatment of Relapses

In cases in which the stools failed to show continued improvement after the veno-clysis was discontinued the skin lost its improved turgor, signs of intoxication reappeared, there was vomiting or abdominal distension, the entire proceedure was repeated. In these cases the period of veno-clysis was shortened usually to 24-30 hours and the return to a maintenance diet stepped up more quickly. In two cases the period of complete withdrawal of fluids orally was reduced to 6 hours instead of 12 and a weak P.P.M. mixture begun immediately thereafter and continued during the veno-clysis without an interval of water diet. Additional blood transfusions were given depending on the condition of the patient. The response to the second veno-clysis seemed slower and less marked than the first.

Feeding

The resumption of feeding following veno-clysis was according to the definite schedule outlined above starting with small quantities two-hourly of a powdered protein or skim milk mixture with saccharine or 5% glucose added. It will be noticed that for the first 24 hours there is a definite scale increase in quantity but following this the adjustment of quantity, interval, and strength depends on the physician's judgment. Powers, Finkelstein and others think this guess work method of feeding far inferior to definite daily caloric increments starting with 50 calories and increasing 25 calories each day, reaching a total diet in 7 to 10 days.

In our series of cases the method of feeding according to the patient's clinical condition was successful and the real

difficulty seemed to be in the proportion of carbohydrate, too large a per cent of glucose or too early addition of dextro-maltose. This affected the frequency of the stools and delayed convalescence. Powdered protein milk 1 in 4 plus saccharine gave the most uniformly satisfactory clinical results especially if continued for several days before making additions of carbohydrate or whole milk. Powdered protein milk plus 5% glucose led to some distension, more frequent stools and slower convalescence. Whole cow's milk plus 5% glucose was entirely satisfactory in one case.

Complications Referable To The Veno-clysis

Hendon, Penfield, Matas and Karelitz have reported the occurence of a chill in some of their cases. There was a rise of temperature, rapid respiration and pulse and cyanosis in some instances. The cause of the reaction was problematical but in most cases thought to be due to one of several causes; New rubber tubing in which there were small foreign particles adhering to the lumen of the tube, due to improper kneading or beating and washing the tube before use. These particles enter the circulation and cause a reaction. This reaction has been noted following intravenous arsenical injections in the treatment of syphilis and was generally traced to the use of new tubing improperly prepared.

A too rapid flow of fluid into the circulation in a short time. Hendon refers to purposely induced reactions in some of his cases due to milking the tube and accelerating the flow.

Further it has been thought that the pH of the solution varying to the side of acidity or alkalinity might be the cause of reactions during intravenous therapy. Penfield conducted a

series of experiments on dogs in which the Ph was varied greatly with no noticeable change in the clinical condition of the animals except in one case where the *pH* was below 4.0. In this case the dog died. Impurity or an acid reaction of glucose may at times give trouble.

The temperature of the solution is now thought to have little bearing on the occurrence of reactions and though formerly various forms of apparatus were devised some of them rather intricate to keep the solution at the point of entrance to the vein at a standard temperature it is now quite common to use a simple apparatus with infusion jar and Murphy drip and tubing and to minimize the importance of the temperature. This is especially true when the flow is only 40-60 cc. an hour by the drop method and where the circulation has an opportunity to warm the solution.

Chemistry of Diarrhoea

Owing to the limitation put on our work, as referred to above, we have no original figures to offer on the chemistry of the body in summer diarrhoea. The subject is well stated and summarized by Cohen together with additional data on his own cases.

The underlying factor in all cases of summer diarrhoea is the loss of tissue and body fluid. Dehydration leads to impaired circulation and secondary functional disturbance in every part of the body. The renal insufficiency is purely functional. This impaired kidney function in association with the dehydration may cause almost complete anuria and this in turn is the main cause of the chemical changes in the blood. Schloss showed there was a rise in the N.P.N. and urea N. of the blood not explained

on the basis of increased concentration of the blood but due to decreased kidney function. Hartman, and Marriott have confirmed these findings though Marriott thought that increased destruction of body protein was an additional factor. Hoag found a rise of N.P.N. in only a few of his cases. The N.P.N. drops with treatment.

Not only is the N.P.N. raised but the blood serum proteins may be increased 50%, (Marriott). Cohen found 4 of his 9 cases had a rise in serum protein. The concentration of the serum protein is not uniform and changes with the stage of diarrhoea, being concentrated early and diluted later in the disease. The determination of the above may not indicate the degree of anhydremia. Decrease in serum protein may cause edema and is a check in the treatment of the case with veno-clysis.

The blood chlorides show a moderate increase though the salts of the blood plasma maintain an approximately normal concentration (Marriott). Treatment with normal saline by veno-clysis does not raise the blood chlorides as stated by Hartman for as Hoag showed on giving sufficient fluid the kidney function is re-established and the blood chlorides do not increase. Hoag and Cohen think the relation between total base and chlorides is important. The base found as bicarbonate increases on giving normal saline and the chlorine decreases. If the total base is reduced and the chlorides increased there may be acidosis. If the base is elevated and the chlorides also raised there is no acidosis.

Marriott and Schloss failed to find an appreciable increase in the ketone bodies in the blood and therefore concluded

that the mechanism of diarrhoeal acidosis was due to retention of waste products from faulty elimination by the kidneys of acid sodium phosphate. Any excretion of fixed base lost in the diarrhoeal stools may be compensated for by the excretion of urinary acids. There may be a decreased CO_2 combining power due to low bicarbonate values. Other blood changes to be noted are increase in concentration of blood volume and increase in specific gravity of blood serum. The *pH* of the blood is not changed except in case of extremis.

Points in Observation of Cases and Effects of Veno-clysis in Treatment

The number of cases treated was 8, falling in the age group between $2\frac{1}{2}$ and 14 months. On admission two were severely toxic, 4 moderately and 2 slightly so, using as a criterion the skin turgor, the mental state, whether alert, drowsy or stuporous, the presence and degree of hypernoea, the condition of the circulation, the number and character of stools and the degree of temperature. It is difficult to judge the degree of intoxication and severity of the disease from clinical examination and the laboratory adjuncts help us but little in diagnosis as to the stage of intoxication.

"All patients with intestinal intoxication are seriously ill and should be treated from the outset on the basis of that fact," Powers. This is shown in our series of 8 cases in which 6 of the little patients who were treated by approved conservative methods from 5 to 15 days became progressively more toxic and dehydrated and veno-clysis had to be resorted to. The last 2 cases of the 8 were therefore started on veno-clysis almost immediately

after admission. Early treatment is particularly important as the longer the patient is in a state of intoxication, the less favorable is the outlook. In the pre-veno-clysis stage the treatment in all cases included the recognized method of water only for a number of hours, then weak feeding mixtures and subcutaneous and intraperitoneal fluid using normal saline or Hartman's solution with 5% glucose. In one case 120 cc. of whole blood was used. Despite this treatment and good nursing care the degree of intoxication advanced in 6 cases and in 2 cases to the point where the patient was practically moribund.

Within a few hours after starting the veno-clysis its effects were noticeable. The infant became quieter, rested better and usually went to sleep. The fever dropped from 1 to 3 degrees in 6 cases and remained down while in 2 cases the drop was temporary until an otitis media was treated but even in the presence of infection the temperature always came down. The stools improved in character, became fewer and remained so, dropping from an average of 8 for 7 cases the 4 days preceeding to 4 the 6 days following the veno-clysis. In three of the cases as a composite, the stools dropped from an average of 9 to 2.6. A decreased number of stools seemed to depend not only on the benefit derived from the rest to the intestinal tract during the veno-clysis but to proper feeding following the veno-clysis as well as to the absence of any infection. In one case the stools dropped from 20 to 2-3 on the first and second day of the veno-clysis but rose again due in all probability to a poorly adjusted after feeding with too much carbohydrate in the mixture. In two cases the tem-

perature failed to stay down until a secondary complication, otitis media had been treated.

The quantity of intravenous fluid given in the different cases in the 24 hours varied between 580 and 960 cc., the average being 821 cc. or 35 cc. per hour, or 68 cc. per pound body weight per day. The amount of fluid given is less than one would expect to give orally and by subcutaneous route. Our cases received only 2.2 ounces of fluid per pound of body weight. During the administration of the veno-clysis 5 patients gained weight, 2 lost and 1 was not weighed. Of those who gained weight the gain varied from 4 ounces to 1 pound, 3 ounces. One case who gained 1.3 pounds had some edema of the head, right eye and face following the second veno-clysis. The other cases gained without any evidence of generalized edema and the gain was well maintained after the veno-clysis was discontinued in 6 cases without any additional fluid being given other than orally, while in 2 cases the weight was maintained by giving only a moderate amount of fluid subcutaneously. This gain in weight with only 821 cc. a day of 5% glucose in normal saline (giving 165 calories per day) shows that there must be some active reparative process going on in the tissues and that the slow administration of intravenous fluid leads to absorption of H_2O by the tissues and replacement (probably) of lost electrolytes. We think that from the results in this series the optimum flow is approximately 80 cc. per pound body weight per 24 hours, or 950 cc. per day which corresponds to the results obtained by Karelitz.

A transfusion was given to five of the eight patients. In three the transfusion followed the first 200 cc. of intravenous fluid using the method of Karelitz. In two a transfusion preceded

the veno-clysis which was subsequently started because of the critical condition of the patient. Two patients received two transfusions. The average size of transfusion was 109 cc. giving approximately 8½ cc. per pound body weight. The transfusion improved the clinical condition of the patient but in the three patients who received no transfusion, two of whom were severely ill, the clinical improvement was equally as satisfactory. From our cases we would conclude that slow intravenous fluid seems to be the most valuable therapeutic aid.

During the veno-clysis the duration of the milk starvation varied between 28 and 40 hours with an average of 35½ hours. A second veno-clysis was thought advisable in three patients and the period of milk starvation was shortened with an average of 25 hours In one case powdered protein milk 1 in 4 plus saccharine was begun 16 hours after the veno-clysis was started, though the veno-clysis was continued for 26 hours. This seemed to prolong the recovery as expressed in the number of stools per day and a slightly longer course than expected. In another case instead of strict starvation during the first of two infusions 3% karo was given 4 hourly during 29 of 39 hours. This definitely aggravated the diarrhoea which had checked within the first half day of the veno-clysis. From these two experiences it suggests itself that milk and carbohydrate starvation should be adhered to during the veno-clysis.

The return to a maintenance diet was accomplished in approximately 14 days in all patients. The addition of carbohydrate or whole milk too early delayed recovery in 2 cases. With the exception of one case in which we used whole cow's milk 2 to 1 plus karo 5%, we used a powdered protein milk mixture in the

proportion of 1 to 4 either with 5% glucose or with saccharine added. In two cases in which powdered protein milk and 5% glucose was used the patient had a relapse and a second infusion was necessary. For treatment of the relapse in these 2 cases powdered protein milk and saccharine were used with better results and we felt that the substitution of saccharine for glucose was preferable for the first few days of convalescence.

Of the eight cases on admission, two had mild complications, one a pharyngitis and tonsillitis with subsequent otitis media, and one rhinitis. A third case developed an otitis media within 24 hours after admission. Of the remaining five patients, all except one showed during their stay in the hospital an otitis media of varying degrees of severity involving either one or both ears. One had a subacute mastoid complicating a right otitis media (not necessitating operation). Troublesome vomiting developed in one little patient. These complications received immediate and prompt treatment, yet despite the undeniable recognized benefit of treatment of parenteral infection on a favorable outcome, we felt the sheet anchor of therapy was veno-clysis and that the parenteral infection was secondary to the debility of diarrhoea and not an etiological factor in its causation in our cases.

Conclusions

1. Continuous intravenous drip or veno-clysis is a safe proceedure which can be used in any hospital.

2. It promises to reduce the mortality in summer diarrhoea from approximately 35% by the most approved methods to as low as 10%. In our cases we had no mortalities.

3. The intravenous route offers numerous advantages of fluid administration and it seems that less fluid is needed by this channel to correct intoxication.

4. Veno-clysis enables withholding fluid and milk orally, gives the gastro-intestinal tract a rest and makes us independent of the intestinal tract for nourishment. A 12-hour water starvation and complete milk and carbohydrate starvation is stressed during the infusion. Emphasis is also placed on a careful resumption of feeding.

5. Blood transfusion is beneficial in all cases but does not seem to be essential for recovery if veno-clysis is used.

6. All cases of intoxication should be considered seriously ill and veno-clysis given early.

Set - Up

Standard - Ajustable

Kelly Warmer enclosing Infusion Jar

Screw Clamp to regulate flow

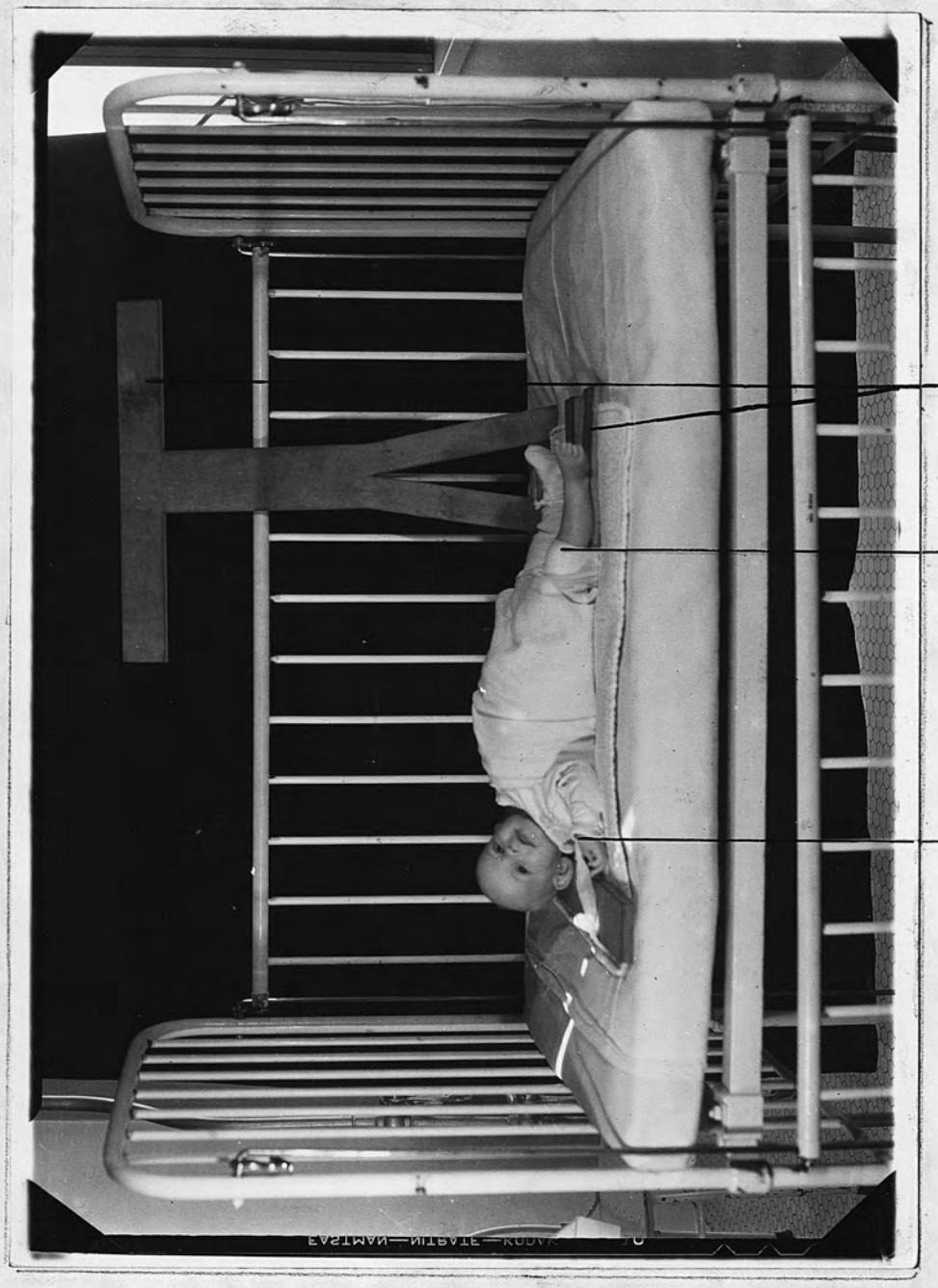
Murphy Drip Bulb

Site of cannula

Sterile Covering Towels

Head of T-Board

Set-Up



T-Board

Immobilization of Leg
(see Text)

Arrangement of Arms

Set - Up

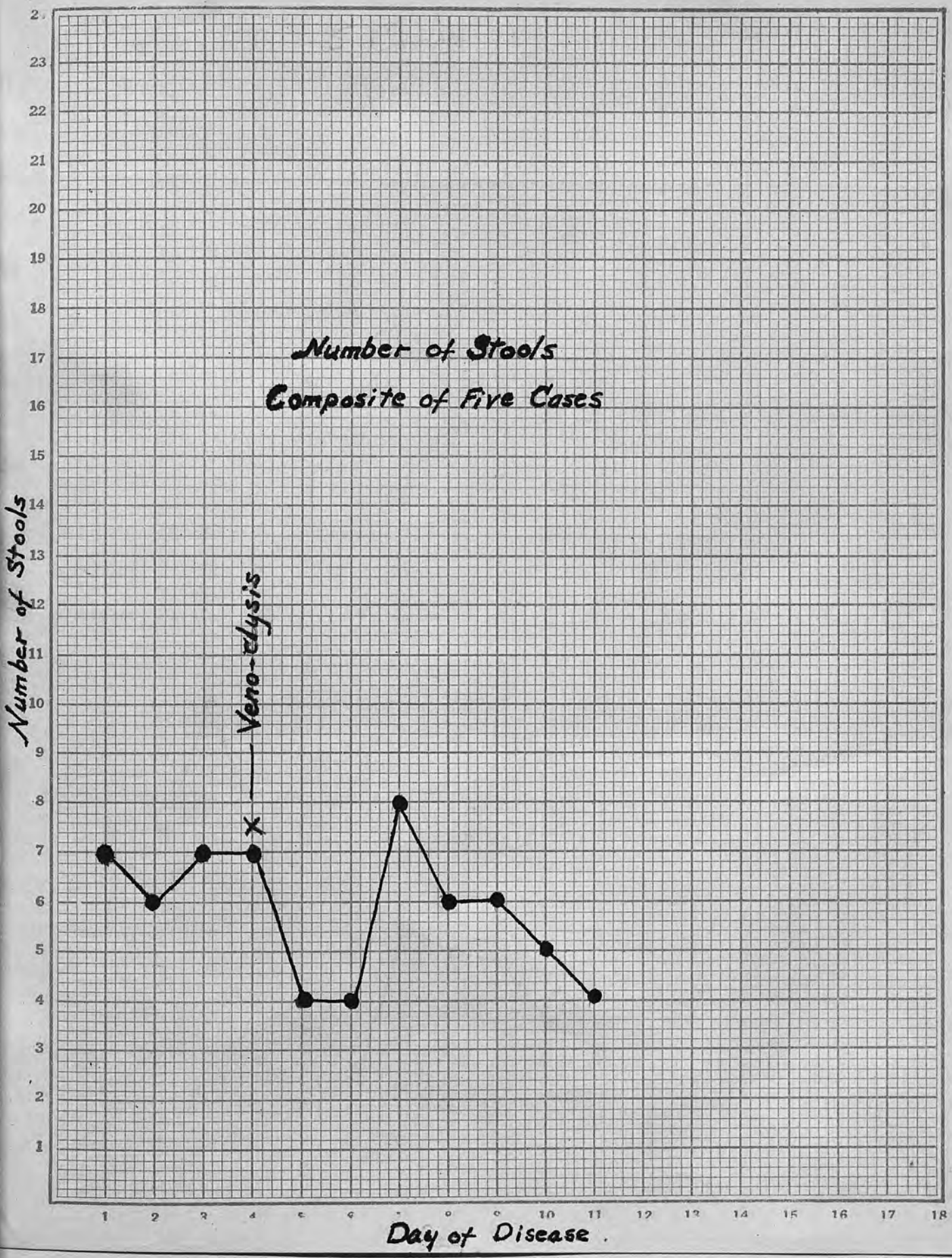
Adaptor - for use in case flow stops

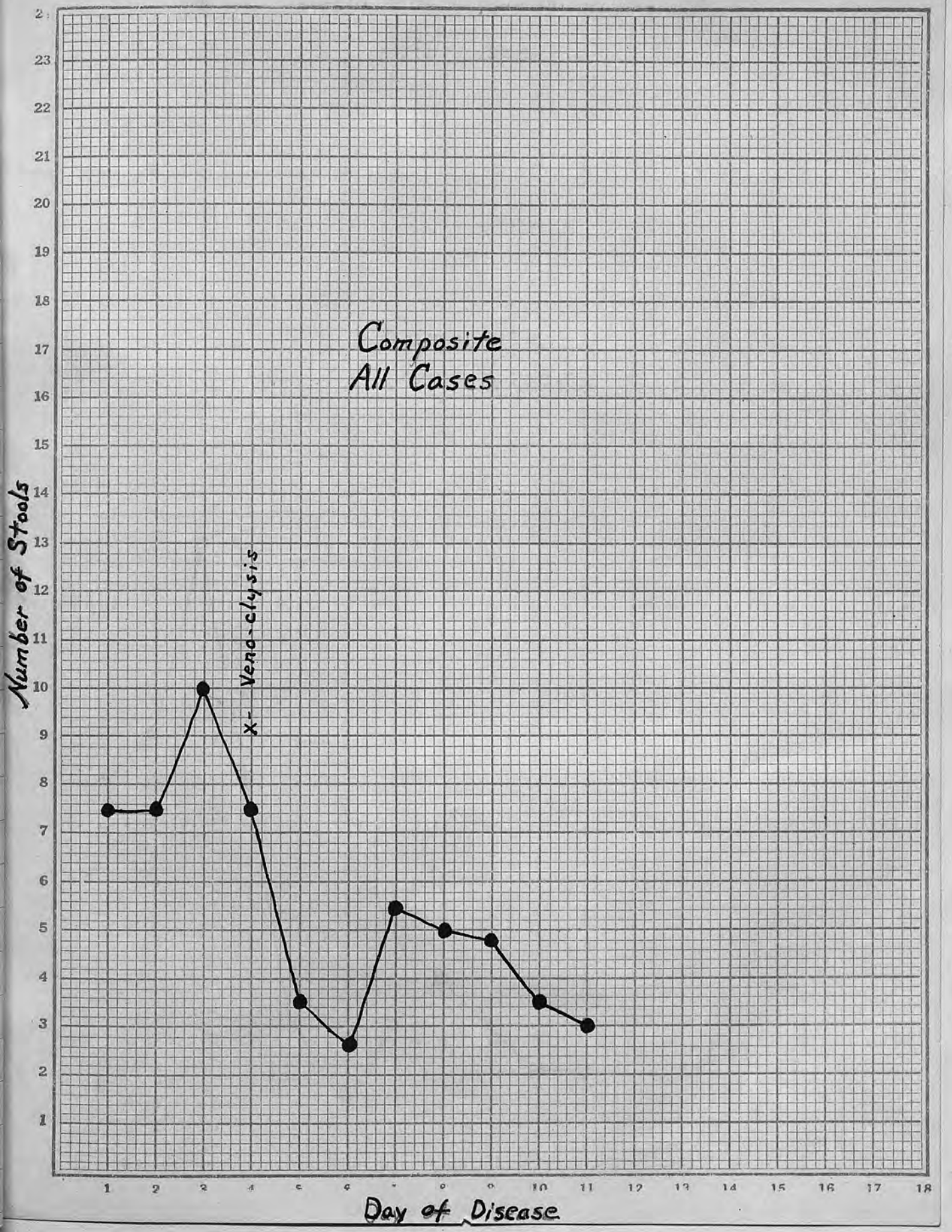
Glass adaptor

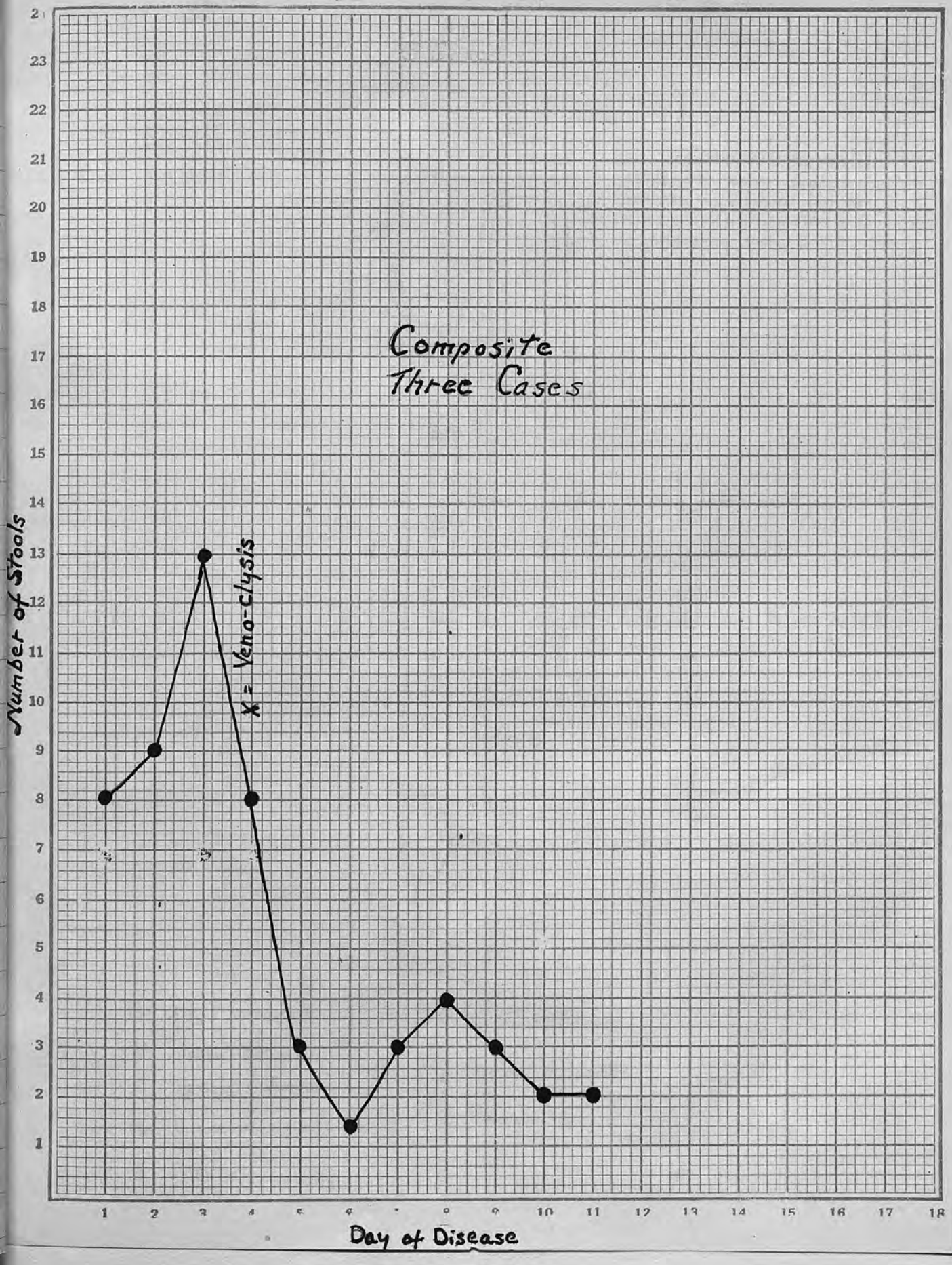
Intravenous - cannula

Needle fixing cannula

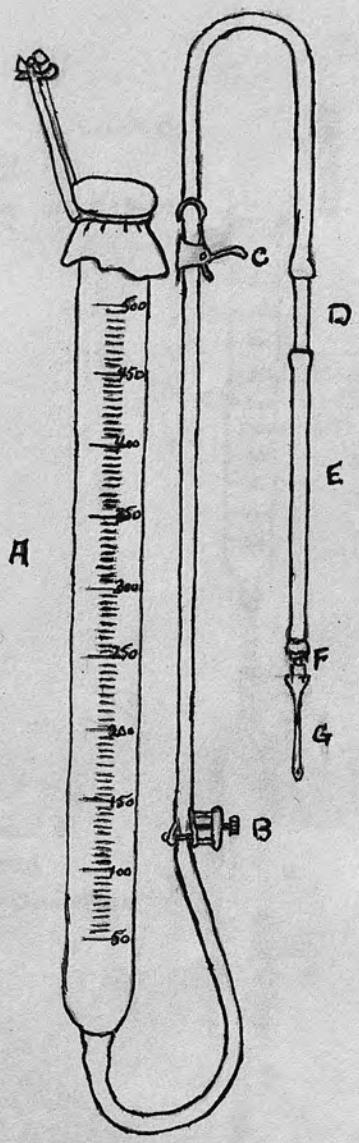
Syringe - for use in case flow stops.

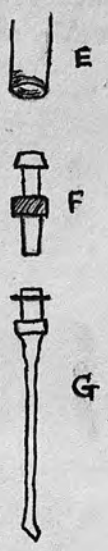

Number of Stools
Composite of Five Cases
Number of Stools
Veno-clysis
Day of Disease


Composite
All Cases
Number of Stools
Day of Disease
X- Vena-clysis


Composite
Three Cases
X = Veno-clysis
Number of Stools
Day of Disease

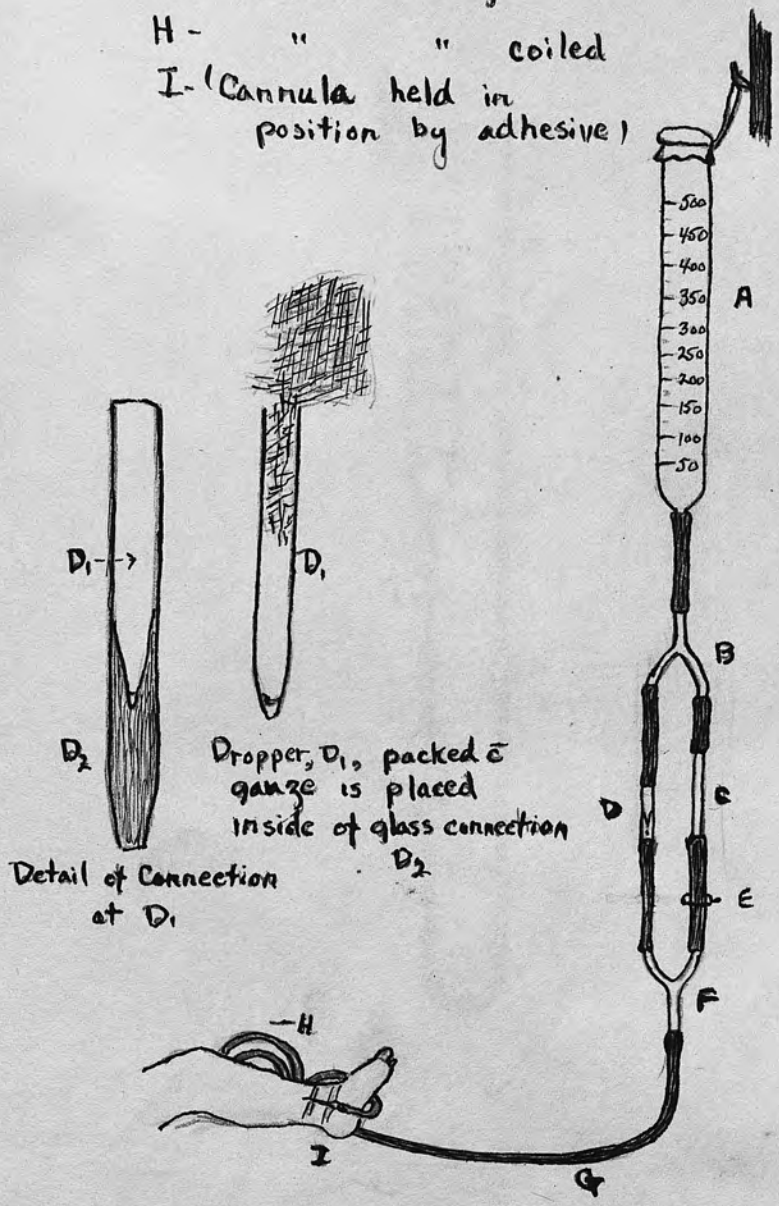
An apparatus commonly used for short infusions hardly suitable for continuous infusions is a Murphy bulb drip.





A. Glass graduate
B. Screw clamp
C. Spring clamp
D. Glass connection
E. Rubber tubing
F. Metal Adapter
G Cannula

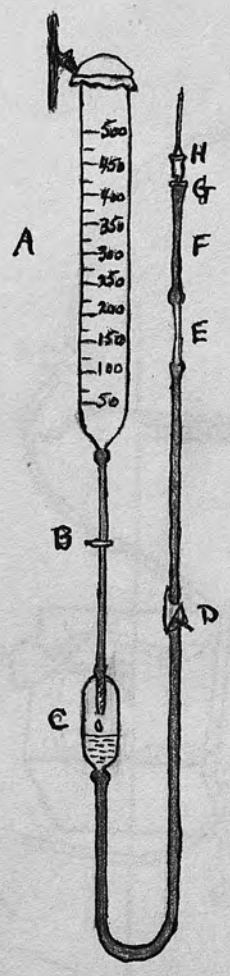
A- Glass Graduate
B- Y tube
C- Glass connection
D- Special glass connection
E- Screw clamp
F- Y tube
G- Rubber tubing
H- " " coiled
I- (Cannula held in position by adhesive)



Detail of Connection at D_1

Dropper, D_1, packed ē gauze is placed inside of glass connection D_2

Effective apparatus devised by Brush for continuous infusion of infants. The glass cannula D is packed ē gauze to deliver a constant specified flow. The coil H next the leg warms the flow thru body heat.

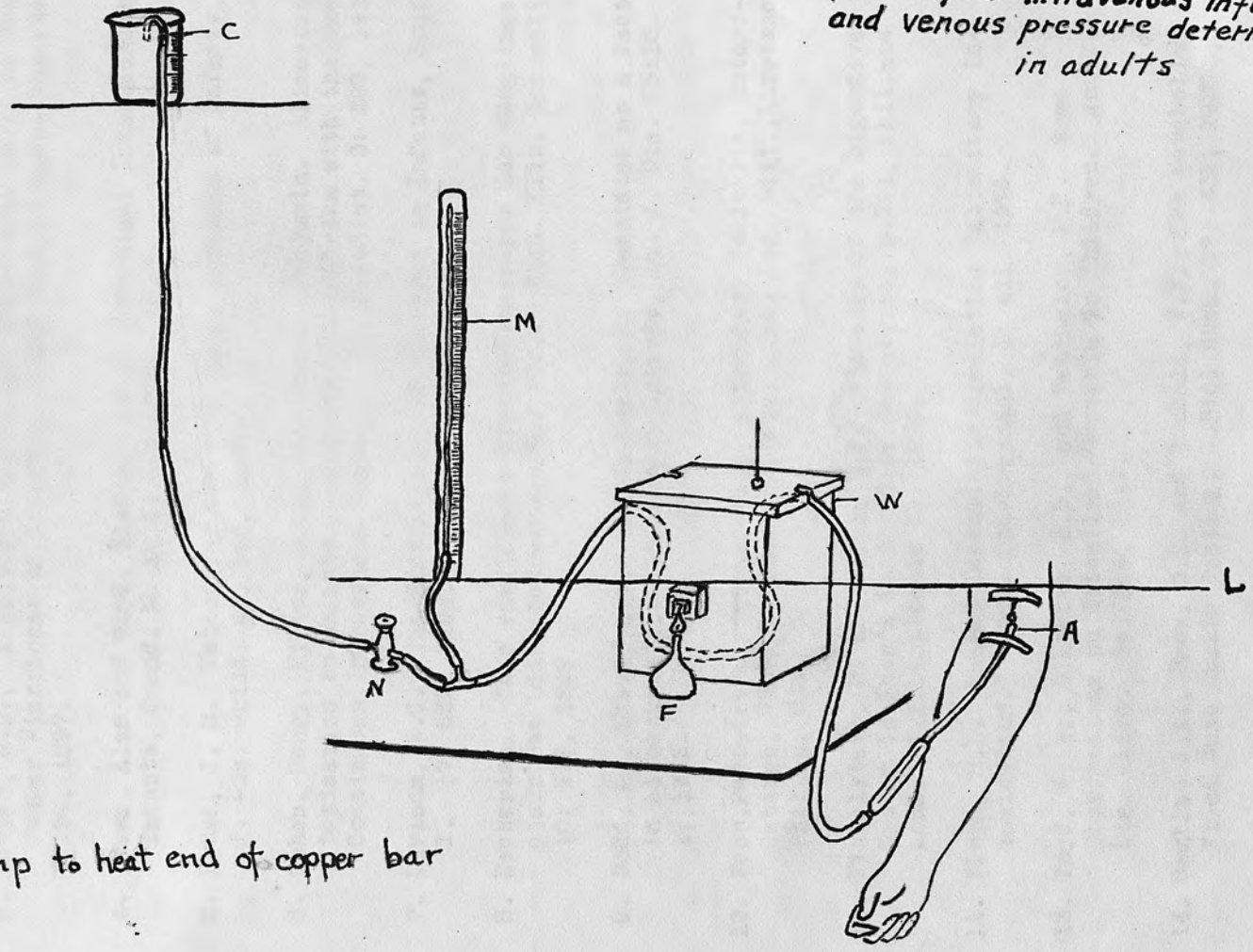


Type of apparatus in general use for continuous infusions. Murphy drip bulb and clamp above act as effective regulators of flow.

Our apparatus shewn in photographs is similar except for a Kelly warmer and infusion jar replacing the graduated cylinder. Our glass connection 'E' fits directly into the cannula in the form of an adaptor.

A- Graduated cylinder
B- Thumb screw clamp
C- Murphy drip bulb
D- Spring Clamp
E- Glass connection
F- Rubber tubing
G- Metal adapter
H- Cannula

Complicated apparatus used by Penfield and Teplitsky for prolonged intravenous infusion and venous pressure determination in adults



N Needle valve
M Manometer
F Alcohol lamp to heat end of copper bar
A Adaptor
L Level
W Box for warming intravenous solution
C Container for intravenous solution

REFERENCES

1. Abt, I.A. (Editor) Year Book of Pediatrics. P.46, Chicago, 1933.

2. Blackfan, K.D., and Maxcy, K.F. Intraperitoneal Injection of Saline, Am. J. Dis. Child. 15: 19, 1918

3. Booker, W.D., A Bacteriological and Anatomical Study of the Summer Diarrhoeas of Infants. Johns Hopkins Hosp. Reports, 6: 159, 1897.

4. Brown, Alan and Boyd, Gladys. Acute Intestinal Intoxication in Infants, Canad. M. A. J., 13: 800, 1923.

5. Brush, J. M. Method for the Continuous Infusion of Infants, Am. J. Dis. Child. 44: 366, 1932.

6. Cohen, Henry, Miller, R.M., and Kramer, Benjamin. Alimentary Intoxication in Infants. Acid Base Equilibrium with the Use of Continuous Intravenous Therapy. The J.Pediat. 3: 299, 1933.

7. Davison, W.C. The Bacteriology of Diarrhea in Infants, South M. J. 17: 552, 1924.

8. Escherich. Uber specifische Krankheitserreger der Säuglings diarrhoen (Streptococcenenteritis). Wien. Klin. Wchuschi., 10: 917, 1897

9. Dodd, K., Minot, A.S., and Casparis, H. Guanidine as a Factor in Alimentary Intoxication in Infants, Am. J. Dis. Child. 43: 1, 1932.

10. Feer, Pediatrics, Intoxication, Alimentary Toxicosis, Entero-Catarrh, Cholera, Infantum, etc. Int. Eng. Edit., Lippincott, Phil. p. 291.

11. Finkelstein, H. and Meyer, L.F. Diseases of the Digestive System in Feer's Textbook of Pediatrics, p.291, Phil.and Lond. J.B.Lippincott Co. 1922.

12. Floyd, M.L. Masked Mastoiditis Simulating "Alimentary Intoxication." Arch. Oto-Laryngal. 1: 411, 1925.

13. Ford, W. W., Blackfan, K.D., and Batchelor, M.D. Some Observations on Intestinal Bacteria in Children. Am. J. Dis. Child. 14: 354, 1917.

14. Gamble, J.L., Ross, G.S. and Tisdall, F.F. The Metabolism of Fixed Base During Fasting, J.Biol.Chem. 57: 633, 1923.

15. Griffith, J.P.C. and Mitchell, A.G. The Diseases of Infants and Children. Vol.II, p.100. Phil. and Lond. W.B. Saunders Co.,1927.

16. Hamilton, B., Kajdi, L., Meeker, D., The Acidosis of Acute Diarrhea in Infancy. Am. J. Dis. Child. 38: 314, 1929.

17. Hartman, A. F., Chemical Changes Occuring in the Body as the Result of Certain Diseases: 1. The Effects of Diarrhoea, Vomiting, Dehydration Oliguria on the Acid Base Balance of the Plasma of Infants with Mastoiditis, Am. J. Dis. Child. 35: 557, 1928.

18. Hartman, A. F. Acidosis, Alkalosis and Dehydration, Colorado Med. 26: 373, 1929.

19. Hendon, G. A. Venoclysis, J. A. M. A. 95: 1175, 1930.
Hendon, G.A. Venoclysis or Intravenous Nutrition, Texas State Med. J. 21: 662, 1926.
Hendon, G.A. Report of Cases Treated by Venoclysis, Kentucky M.J. 27: 202, 1929
Hendon, G.A. Experiences with Venoclysis, Ann.Surg. 91: 753, 1930.

20. Henoch, Edward. Lectures on Diseases of Children, N.Y. Wm.Wood & Co., 1882, p. 56, 56, 200 and 207.

21. Hoag, L.A. and Marples, Eleanor. Acid Base Status in Dehydration Accompanying Diarrhea in Infants. Effect of Treatment with Parenteral Fluids, Am.J. Dis.Child., 42: 291, 1931.

22. Holt, L. E., and Howland, John. Diseases of Infancy and Childhood. 9th Ed., p. 276. N.Y. and Lond. D. Appleton & Co.1929

23. Horsley, J. S. and G. W. Continuous Intravenous Injection of Dextrose in Ringers Solution. Arch. Surg. 22: 86, 1931.

24. Howell, W. H. Textbook of Physiology 10th Ed., 1927, p.573. Phil. & Lond. W.B. Saunders & Co.

25. Howland, John and Marriott, W. Acidosis Occuring with Diarrhea, Am. J. Dis. Child. 11: 309, 1916.

26. Jones, B. B. Iso-Agglutinins in the Blood of Newborn, Am.J.Dis. Child. 22: 586, 1921.

27. Karelitz, Samuel and Schick, Bela. Treatment of Alimentary Toxicosis. J.A.M.A. 99: 366, 1932.

28. Karelitz, Samuel. Treatment of Toxicosis with the Aid of a Continuous Intravenous Drip of Dextrose Solution, Am. J. Dis. Child. 42: 781, 1931.

29. Kendall, A. I. The Relation of Bacteria to the Etiology of Summer Diarrhoea in Young Children, Boston M. & S. J. 172: 851, 1915.

30. Marriott, W. McKim, Anhydremia, Physiol. Rev. 3: 275, 1923.

31. Marriott, W. McKim. Further Observations Concerning the Nature of Nutritional Disturbance. Tr. Am. Ped. Soc. 37: 38, 1925.

32. Matas, Rudolph. The Continued Intravenous Drip, Ann.Surg. 79: 643, 1924.

33. Miller, Reginald. Acute Infective Diarrhoea (Acute Gastro-Enteritis: Cholera Infantum) in: Diseases of Children. Edited by Garrod, Batten, Thursfield and Paterson. N.Y., Wm.Wood & Co., 1929.

34. Morgan, H. DeR. Upon the Bacteriology of the Summer Diarrhoea of Infants. Brit. M.J. 1: 908, 1906.

35. Penfield, W. S. and Teplitsky, David. Prolonged Intravenous Infusion and the Clinical Determination of Venous Pressure, Arch. Surg. 7: 111, 1923.

36. Porter, L., and Carter, W. E. Management of the Sick Infant, "Diarrhoea," 3rd Ed. p.39, C.V. Mosby Co., St. Louis, 1922.

37. Powers, G. S. A Comprehensive Plan of Treatment for the So-called Intestinal Intoxication of Infants, Am. J. Dis. Child. 32: 232, 1926.

38. Ravenel, S. F. The Hazards of Intraperitoneal Injections, J.A. M. A. 100: 473, 1933.

39. Robertson, Bruce, Brown, Alan and Simpson, Roy. Blood Transfusion in Children, Its Indications and Limitations. From an Analysis of 600 Cases. Northwest Med. 20: 233, 1921.

40. Robertson, Bruce. Blood Transfusion in Severe Burns in Infants and Young Children, Canad. M.A.J. 11: 744, 1921.

41. Schloss, O.M. Intestinal Intoxication in Infants. The Importance of Impaired Renal Function. Am. J. Dis. Child. 15: 165, 1918.

42. Schloss, O. M. and Stetson, R.E. The Occurrence of Acidosis with Severe Diarrhea. Am. J. Dis. Child. 13: 218, 1917.

43. Sidbury, J.B. Transfusion in Infancy and Childhood, J.A.M.A. 89: 855, 1927.

44. Talbot, F. B. The Use of Glucose in the Treatment of Disease in Children. Boston M. & S. J. 192: 1000, 1925.

45. Tenbroech, C. and Norbury, E.G. The Presence of B. Dysenteriae, B. Proteus vulgaris, B. Welchii and Morgan's bacillus #1, in the Stools of Cases of Infectious Diarrhea, Boston M. & S. J. 173: 280, 1915.

46. Thompson, John. The Clinical Study and Treatment of Sick Children, p.200, Edinburgh, Oliver and Boyd, 1925.

47. Tisdall, F. F., Drake, T.G.H., and Brown, Alan. The Carbohydrate Metabolism of the Normal Infant, Am. J. Dis. Child. 30: 675, 1925.

48. Underhill, F. P. and Sallick, A. On the Mechanism of Water Intoxication, J. Biol. Chem. 63: 61, 1925.

49. Woodyatt, R. T., Sansum, W.B. and Wilder, R. M. Prolonged and Accurately Timed Intravenous Injections of Sugar: A Preliminary Report, J.A.M.A. 65: 2067, 1915.

THE EFFECT OF CONTINUOUS VENO-CLYSIS IN THE TREATMENT OF INTESTINAL INTOXICATION IN INFANTS

John L. Law